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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/251,073
Filing Date: February 16, 1999
Appellant(s): LOBB ET AL.

For Appellant
Louis Myers

EXAMINER'S ANSWER

This is in response to the appeal Brief filed 3/24/04.

The text of those sections of Title 35 U.S. Code not included in this appeal can be found in a previous Office Action herein.

(1) Real Party of Interest.

A statement identifying the real party of interest in contained in the Brief.

(2) Related Appeals and Interferences Identified.

A statement identifying that no related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the Brief.

(3) Status of Claims.

The statement of the status of claims contained in the Brief is correct.

Claims 1-3, 6, 7, 9-13, 17, 18 and 26-37 are rejected.

Claims 4, 5, 8, 14-16 and 19-25 have been canceled.

(4) Status of Amendments After Final.

Appellant's statement of the status of amendments contained in the Brief is correct.

(5) Summary of Invention.

The summary of invention contained in the Brief is correct.

(6) Issues.

Appellant's statement of the issues in the Brief is correct.

(7) Grouping of Claims.

The examiner is in agreement with appellant's statement that claims 1-3, 7, 9-13, 17, 18 and 26-37 stand or fall together.

(8) Claims Appealed.

The copy of the appealed claims contained in the Appendix to the Brief is correct.

(9) Prior Art of Record.

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

A) Arrhenius et al., U.S. Patent No. 6,117,840.

B) Kogan et al., U.S. Patent No. 5,510,332.

C) Wayner et al., U.S. Patent No. 5,730,978.

(10) Grounds of Rejection.

The following ground(s) of rejection are applicable to the appealed claims.

Rejection Under 35 U.S.C. § 103

Claims 1-3, 6, 7, 9-13, 17, 18 and 26-37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Wayner et al. (U.S. Patent No. 5,730,978) AND/OR Kogan et al. (U.S. Patent No. 5,510,332) AND/OR Arrhenius et al. (U.S. Patent No. 6,117,840) in view of art known of the nature and treatment of asthma at the time the invention was made as acknowledged in the Background of the Invention on pages 1-3 of the instant specification and pages 7-8 of the instant specification essentially for the reasons of record set forth in the previous Office Action.

Wayner et al. teach methods of suppressing the immune response in human patients, including chronic and relapsing inflammation, including asthma by interfering the binding of receptor-ligand interactions between lymphocytes and endothelial cells (see Utility of the Invention, columns 15-17, including column 16, paragraph 1). Here, the inhibitory peptides may be administered by any route, including intravenously, intranasal and oral (column 16, paragraph 2 - column 17, paragraph 1). Wayner et al. teach that the inhibitory peptide comprising fibronectin, a portion of fibronectin including the fibronectin alternatively spliced IIICS region including the CS-1 domain comprising the EILDV motif which blocks adhesive events, including those with $\alpha 4\beta 1$ expressing lymphocytes and endothelial cells (see entire document, including Fibronectin, columns 3-7; Summary of the Invention, column 7-8; Detailed Description of the Invention, including columns 10 - 17 and Examples).

In addition to the teachings of treating asthma, Wayner et al. also teach treating allergy as well as asthma (e.g., see Summary of the Invention, including column 7, paragraph 2 and Utility of the Invention, including column 16, paragraph 1).

Kogan et al. teach methods of treating diseases associated with uncontrolled migration of white blood cells to damaged tissues such as asthma by inhibiting the binding of $\alpha 4\beta 1$ to VCAM-1 and that the means for determining effecting inhibiting amounts were well known in the art (see Process of Inhibiting the Binding of $\alpha 4\beta 1$ Integrin to VCAM-1, columns 9-10). Here, the pharmaceutical compositions could be administered to humans

by intravenous injection of intranasally via a spray or aerosol (see Pharmaceutical Composition; columns 8-9). Kogan et al. teach that α4β1 recognizes fibronectin, including fibronectin isoforms including the CS1 peptide present in the alternatively spliced type III connecting segments (see Detailed Description of the Invention, including The Invention on column 3 and Peptides on columns 3-8 and Examples, including SEQ ID NO: 101)

In addition to the teachings of treating asthma, Kogan et al. also teach treating allergy as well as asthma (e.g. see columns 9-10, overlapping paragraph).

Arrhenius et al. teach methods of blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. α4β1) to inhibit inflammatory responses, including asthma, asthmatic lung (see Compositions and Process, columns 24-28). Here, the pharmaceutical compositions are administered in the manner of administration of the particular disease being treated and its severity, including parenteral and local administration such as aerosol in amounts of about 0.25 mg to about 25 mg and about 1 mg/kg/day to about 500 mg/mg/kg/day of the inhibitor peptide, including prophylactically treating patients at risk (see columns 25-28). Arrhenius et al. teach the use of fibronectin and fibronectin derived peptides such as CS-1 and SEQ ID NO: 3 to block various inflammatory conditions by blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. α4β1) (see entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention).

In addition, Arrhenius et al. disclose Example 5 on treating asthmatic rabbits, which rely upon early phase and late phase allergic reactions (see Example 5 on columns 33-34).

Therefore, Wayner et al., Kogan et al. and Arrhenius et al. all recognized treating both asthma and allergy at the time the invention was made with fibronectin inhibitors.

The well known practices of the ordinary artisan in the treatment of asthma, including allergen-induced asthma at the time the invention, was consistent with the treatment of asthma of fibronectin-derived inhibitors which block the interactions between $\alpha 4\beta 1$ and its receptor between lymphocytes and endothelial cells in order to inhibit inflammatory responses as taught by Wayner et al., Kogan et al. and/or Arrhenius et al. These references are consistent with the acknowledged art in the instant specification as filed that effective dosages of inhibitors are provided in the manner of administration of the particular disease being treated and its severity and the patient's needs, including intravenous and aerosol over a broad range of dosages.

One of ordinary skill in the art at the time the invention was made would have been motivated to select fibronectin-derived peptides, including those comprising EIDLV to treat asthma, including allergen-induced asthma by inhibiting the interaction between lymphocytes and endothelial cells. Given the art known course and treatment of asthma which undergoes acute and chronic phases in responses to allergens, one of ordinary skill

in the art would have been motivated to treat asthmatic patients prior to, during and after allergen exposure with the dosages encompassed by the claimed invention. It was routine for the ordinary artisan in asthma would have manipulated the appropriate dosings and modes of administrations to meet the needs of the patients and the course of the disease at the time the invention was made.

The claimed timing of administration and effective dosages were well known in the art, as the ordinary artisan would have applied fibronectin inhibitors to achieve the therapeutic endpoint of diminishing inflammatory conditions in asthmatic patients, including allergen-induced asthmatics. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(11) Response to Argument

Rejection Under 35 U.S.C. § 103

Appellant's arguments have been fully considered but are not found persuasive essentially for the reasons of record.

Appellant asserts that nothing in the prior art of record would have led the artisan to pick and choose the specific aspects from th references and modify them to administer a soluble fibronectin polypeptide to a patient suffering from allergic asthma.

Appellant acknowledges that both Wayner (e.g. column 16, lines 17-26) and Kogan (e.g. column 2, lines 3-7) disclose diseases that might be treated by inhibiting $\alpha 4\beta 1$ integrin binding.

However, appellant submits that neither Wayner nor Kogan provide any in vivo data or animal models to support a conclusion that administration the claimed compound, i.e., a soluble fibronectin polypeptide, would effectively treat asthma, much less allergic asthma, as required by the claims. In addition, appellant acknowledges that while Wayner and Kogan disclose a variety of potential diseases that could be treated by inhibiting $\alpha 4\beta 1$ binding, appellant asserts that nothing in Wayner and/or Kogan provides motivation to one of skill in the art to specifically administer a soluble fibronectin polypeptide for the treatment of allergic asthma.

Appellant further asserts that one of skill in the art would not reasonably expect that a single compound, e.g. a soluble fibronectin polypeptide, would be successful in the treatment of all of the diseases, or even most of the diseases, disclosed in Wayner and Kogan. Appellant notes that Wayner and Kogan, at most, only provide in vitro data.

Appellant asserts that Arrhenius fails to make up for the deficiencies of Wayner and Kogan. Appellant submits that while Arrhenius disclose in vivo data demonstrating a treatment of asthma with peptidomimetic agents, such treatment does not use soluble fibronectin polypeptides, as required by the claims. For example, Arrhenius et al. disclose Example 5 on treating asthmatic rabbits with a peptide inhibitor, which relies upon early phase and late phase allergic reactions (see Example 5 on columns 33-34).

In contrast to applicant's assertions that Arrhenius teaches away from fibronectin polypetides such as CS-1, disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. See In re Susi USPQ 423 (CCPA 1971). A known or obvious composition does not patentable simply because it has been described as somewhat inferior to some other product for the same use. See In re Gurley 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See MPEP 2123.

Even though Arrhenius et al. disclose the costliness of CS-1 polypeptides, the fact that a combination would not be made by businessmen for economic reasons does not mean that a person of ordinary skill in the art would not make the combination because of some technological incompatibility. In re Farrenkopf , 713 F.2d 714, 219 USPQ 1 (Fed. Cir. 1983).

Further, it is noted that column 4, paragraph 5 of Arrhenius et al. disclose:

"The role of VLA-4 and the CS-1 peptide in various chronic and acute immunoinflammatory disease states having been established, it would be of importance if compound could be found that inhibit VLA-4 lymphocyte interaction and were other than anti-VLA-4 antibodies that can themselves induce an immune response on repeated administration or the CS-1 peptide that is large and costly to make, and also is subject to rapid degradation. The disclosure that follows describes such small molecules that are more potent that is CS-1 itself."

Also, it is noted that Arrehnius et al. describes the contemplated peptides as mimics of the whole fibronectin molecules or at least the 25 residue CS-1 portion of fibronectin that binds to VLA-4 (see column 8, lines 48-52 of Arrhenius et al.).

Therefore, Arrhenius et al. teach that the role of inhibiting VLA-4-mediated interactions, including the use of fibronectin derived peptides such as CS-1 peptide in various chronic and acute immunoinflammatory disease states has been established and that the disclosed peptidomimetics are contemplated to mimic the inhibitory and immunosuppressive CS-1 peptide.

As pointed out previously and herein, Arrhenius et al. provides a clear teaching of methods of blocking interactions between the fibronectin derived peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) to inhibit inflammatory responses, including asthma, asthmatic lung (see Compositions and Process, columns 24-28). Arrhenius et al. teaches the use of fibronectin and fibronectin derived peptides such as CS-1 and SEQ ID NO: 3 to block various inflammatory conditions by blocking interactions between the fibronectin peptide CS-1 and VLA-4 (i.e. $\alpha 4\beta 1$) (see entire document, including Background of the Invention, Summary of the Invention and Detailed Description of the Invention).

In addition, given the disclosure of Arrhenius et al., including Example 5 on treating asthmatic rabbits, which rely upon early phase and late phase allergic reactions (see Example 5 on columns 33-34) and the common immunosuppressive properties of the referenced peptide mimics and fibronectin derived peptides; one of ordinary skill in the art would have recognized the applicability of CS-1 as well as the referenced peptidomimetics that serve to mimic CS-1 in the treatment of allergic asthma with an expectation of success at the time the invention was made.

In addition, both Wayner et al. and Kogan et al. provide clear direction and motivation to employ the fibronectin polypeptides in the treatment of asthma and allergy at the time the invention was made.

Here in contrast to appellant's assertions of teaching away by the prior art because Arrhenius et al. teach asserted advantages of peptide mimics over the previously known immunosuppressive anti-VLA-4 antibodies and fibronectin derived CS-1, these peptide mimics were contemplated to mimic CS-1 itself (see column 8, lines 48-52 of Arrhenius et al.). Further, each of Wayner, Kogan and Arrhenius teach the broad applicability of CS-1 as an anti-inflammatory in a variety of conditions, including allergy and asthma at the time the invention was made. In contrast to appellant's position, there was no discouragement nor skepticism in the prior art in the applicability of the inhibitory CS-1 peptide to treat a variety of inflammatory conditions in the prior art.

The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01(C). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

Appellant has not provided objective evidence to support the asserted inadequacies of the prior art references. Here, the claimed and prior art methods rely upon the administration of soluble fibronectin polypeptides to inhibit binding of receptor-ligand interactions (i.e. $\alpha 4\beta 1$ mediated interactions) between leukocytes and endothelial cells as well as the migration of white blood cells to damaged tissues in inflammatory conditions such as asthma and allergy. There appears to be no manipulative differences between the prior art and the instant methods in the steps of inhibiting inflammatory responses, such as asthma, allergy or allergic asthma. Further, appellant has not provided any objective evidence that distinguishes the inhibitory and anti-inflammatory properties of the prior art fibronectin derived peptides in the same or nearly the same targeted inflammatory diseases and conditions. The prior art teaches the use of the same anti-inflammatory fibronectin peptides as claimed to achieve the same anti-inflammatory therapeutic endpoints by the same mechanism of action for the same reasons as the claimed invention.

Also, as pointed out previously the prior art teachings are consistent with the Background of the Invention. The triggers that have been found to induce airway hyperresponsiveness in asthma include inhaled allergens, inhaled low molecular weight agents to which the subject has become sensitized, viral or mycoplasma respiratory infections, and oxidizing gases (page 1 paragraph 4 of the instant specification). Here, it is acknowledged that the common feature of inducing triggers is that they are associated with airways inflammation, inciting triggers produce smooth muscle contractions which

depend on the underlying degree of hyperresponsiveness rather than increasing airways responsiveness themselves.

Therefore, in contrast to appellant's assertions, one of ordinary skill in the art recognized the known and prevalent contribution of allergens to the natural history of asthma, including early and late phase responses in allergen-induced asthma, as well as the common feature of inducing triggers (e.g. allergen) at the time the invention was made (see pages 1-3 of the instant specification). In turn, the prior art teaching of treating both asthma and allergy as well as the description of a model that exemplifies allergic allergy in the context of peptides that mimic fibronectin peptides (e.g. see Example 5 of Arrhenius discussed above) provided ample motivation and expectation of success in treating asthmatic allergy to the ordinary artisan at the time the invention was made. The ordinary artisan would have immediately envisaged the treatment of allergic asthma with fibronectin derived peptides, given the prior art teachings of the treating asthma and allergy as well as exemplifying an allergic asthma model. The obviousness of such treatment is further bolstered by the known prevalent contribution of allergens to asthma and targeting the common responses to inducing triggers in asthma (e.g. allergens) by the ordinary artisan at the time the invention was made.

One of ordinary skill in the art at the time the invention was made would have been motivated to select fibronectin-derived polypeptides, including those comprising EIDLV, to treat allergen-induced asthma by inhibiting the interaction between lymphocytes and endothelial cells. Given the art known course and treatment of asthma which undergoes acute and chronic phases in response to allergens, one of ordinary skill in the art would have been motivated to treat asthmatic patients prior to, during and after allergen exposure with the dosages of fibronectin derived polypeptides encompassed by the claimed invention.

Appellant's arguments are not found persuasive

(12) For the above reasons, it is believed that the rejections should be sustained.

Respectively submitted,

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